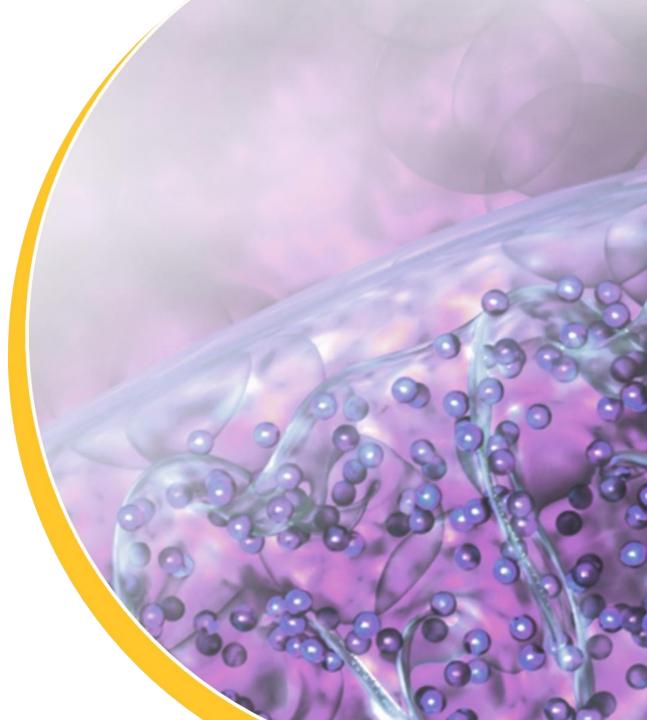
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Novel Oral Therapy Significantly Improving Muscle Quality

Increasing Fast Twitch Muscle Strength & Function Addressing Pathologic Sarcopenia



Progress Highlights





Ph 1 IND accepted - Enrollment Initiation Q4 '24

• Ph 1 data readout with Target Engagement Biomarker Q3 '25

Characterized MF-300's Potential Human Benefit

- Translation of MF-300 muscle benefit supported by Scholar Rock Ph 3 readout (SMA)
- Proteomic analysis identifies potentially relevant translational effects of MF-300
- Established PGE2-responsive human myocyte assay to test mechanistic hypotheses

Correlated PD Biomarker to Target Dose Efficacy

- PGE-MUM highest correlation with MF-300
- TD* of 10mpk potential for circulatory biomarker tied to grip strength in aged population

Ph 2a Sarcopenia Study Plan: Transformational Value Opportunity

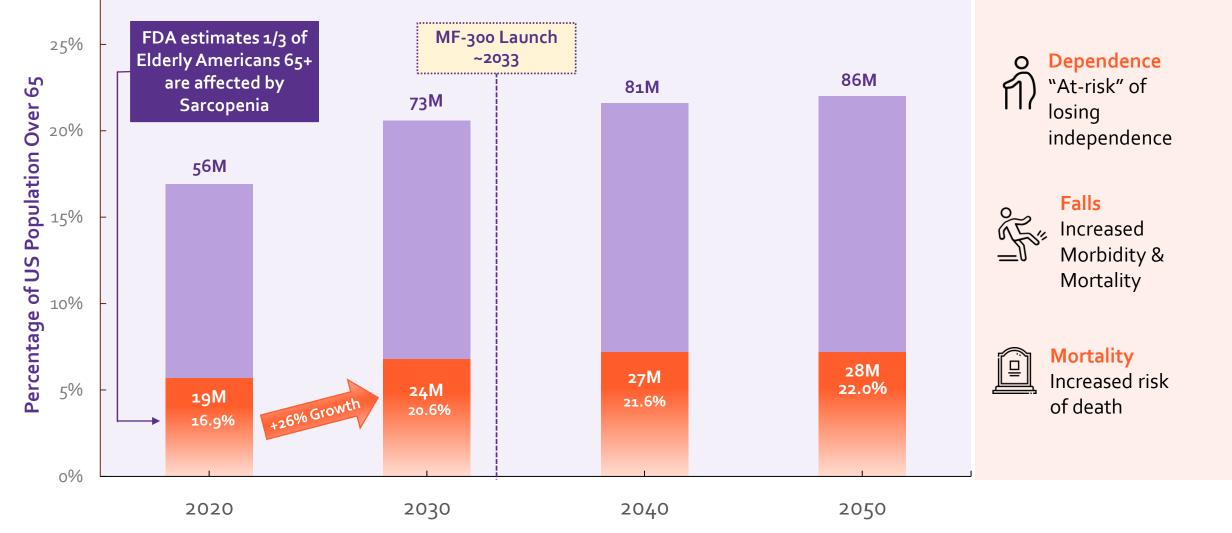
- Efficacy study: <u>PE</u>* SPPB, QOL, Muscle Function & Disease Response Biomarker(s)
- Expecting first patient dosed Q4 '25 with data readout H2 '26
- Engaged with key stakeholders on registrational primary endpoints

TD= Target Dose PE = Primary Endpoint SPPB = Short Physical Performance Battery QOL= Quality of Life

Sarcopenia: Large Unmet Medical Need with No FDA Approved Therapy

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Current U.S. Healthcare Sarcopenia Spending Estimated >\$40 Billion Annually



Source: Burns ER, J. Safety Res. 2016, U.S. Population est. 331M

Diminished Muscle Quality is a Root Cause of Sarcopenia

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Sarcopenia

- Severe loss of muscle strength and mass with aging
- Strength declines faster than muscle mass¹ due to Diminished muscle quality⁵
 - Existing muscle is weaker, contracts slower
 - Disproportionate loss of fast twitch muscle force
 - Progressive denervation of muscle
 - **Reduced regenerative potential** of muscle stem cells
- Age induced inflammation, Inflammaging, is a key driver of reduced muscle quality and muscle weakness⁴

¹Cruz-Jentoft and Sayer, *Lancet* 2019 ²Jubrias and Conley, *Fun. Neurobio. of Aging*, 2001 ³Li et al., *Med Sci Sports & Exercise*, 2017 ⁴Heinze-Milne et al., *Mech Aging Dev*, 2022 ⁵Mohien et al., *eLife*, 2019

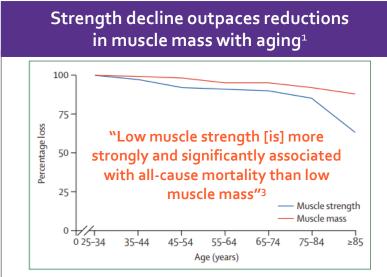


Figure 1: Percentage loss of muscle mass and muscle strength with age in men

Reduction in Muscle Quality Contributes >30% to Loss in Muscle Force in Elderly²



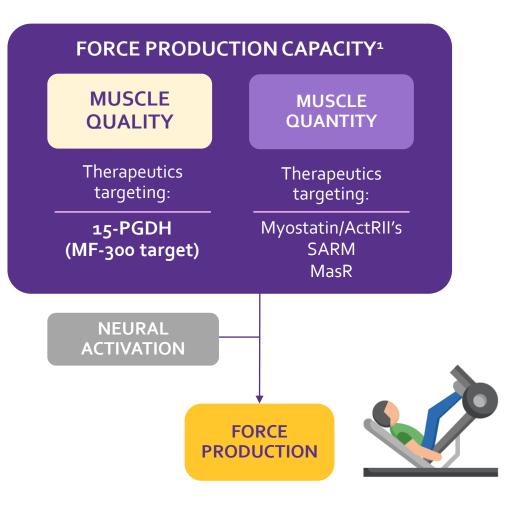
Improving Muscle Quality in Sarcopenia: Differentiated Therapeutic Approach

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"Maintaining or gaining muscle mass does not prevent aging-associated declines in muscle strength"²

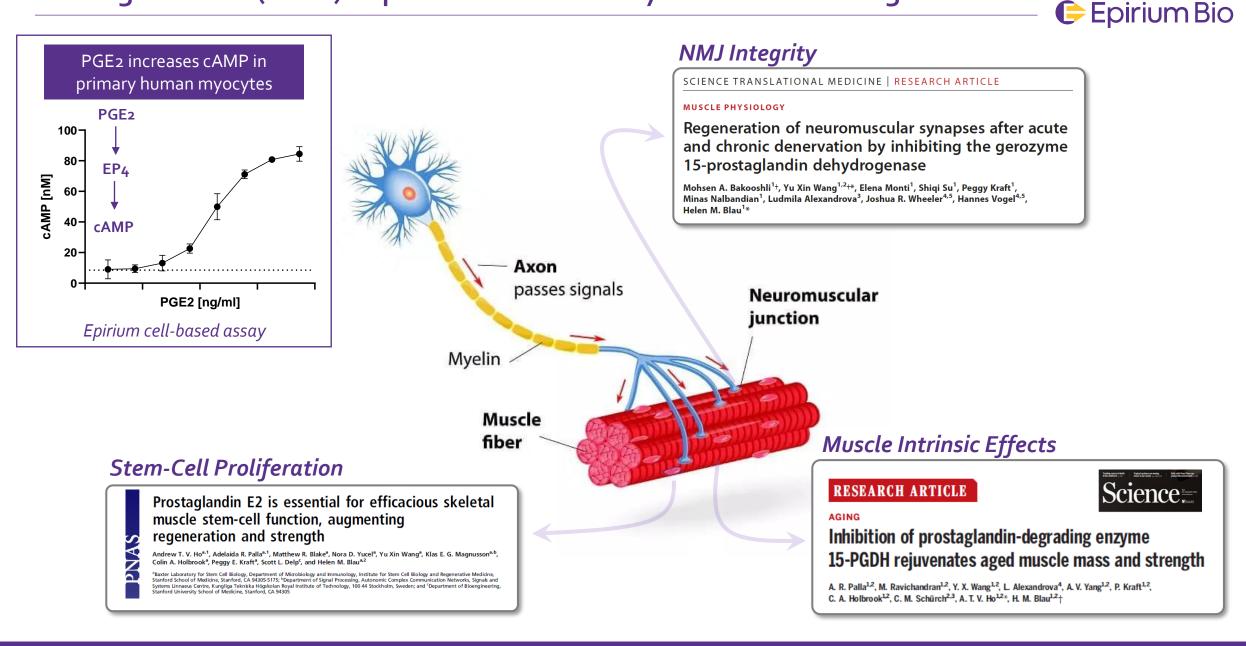
MF-300: First-in-Class Oral Therapy Improving Muscle Quality

- Broad applicability in aging
- Differentiated from adding muscle quantity
- Combination Tx potential



¹ Adapted from Jubrias and Conley, *Fun. Neurobio. of Aging*, 2001 ² Goodpaster et al., *J Gerontology*, 2006

Prostaglandin E2 (PGE2) Improves Muscle Quality and Function in Aged Mice

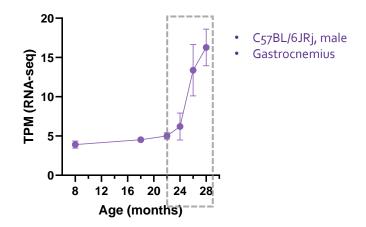


MF-300 Target: 15-PGDH Upregulated in Aging Muscle, Correlated w/ Strength Loss

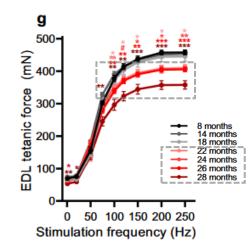


Aged Mice: 15-PGDH elevated

Muscle 15-PGDH gene expression (Hpgd) increases during aging¹



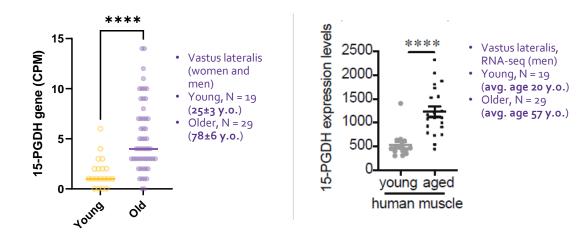
Muscle strength declines during window of elevated Hpgd²



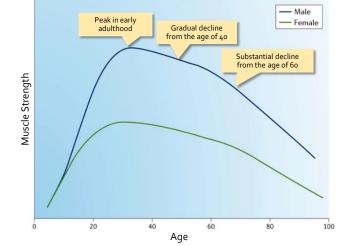
¹ https://sarcoatlas.scicore.unibas.ch/ GSE145480, ² Borsch et al., Com Bio 2021

Elderly Humans: 15-PGDH elevated

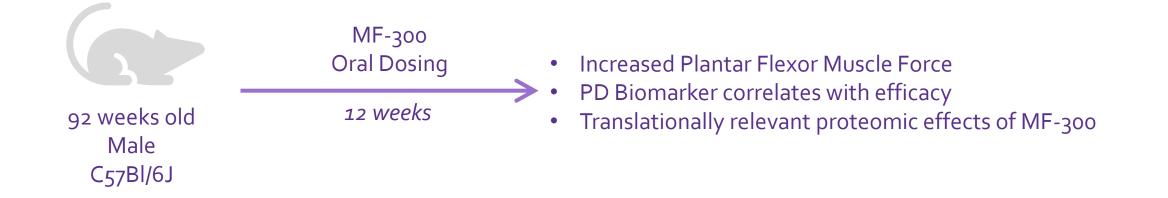
15-PGDH gene expression is elevated with aging in human muscle^{3,4}



Grip strength, a predictor of sarcopenia risk, declines with age⁵



3 GEO167186, 4 Raue et al., J Appl Physiol 2012 (published in Palla et al., Science 2021), 5 Dennison et al., Nat Rev Rheum 2017



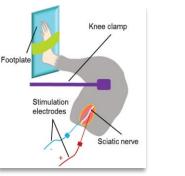
In vivo & ex vivo isometric force measured with a 305C muscle lever system (Aurora Scientific Inc., Aurora, CAN)

Reproducible results

- Defined stimulation parameters (amplitude, frequency, duration)
- Independent of fear driven motivation (e.g., grip, rotarod, wire hang)
- Measure several parameters of muscle function
 - Absolute force, contraction rate, relaxation rate, force/frequency response

In vivo Plantar Flexor Force Mixed fiber type

Ex vivo EDL Force Fast twitch





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MF-300 Substantial Efficacy at Target Dose w/ Correlated PD Biomarker



MF-300: Repeated efficacy (muscle force) at Target dose across multiple studies in mice ≥90 weeks old

Study #	Mouse Strain, Age	Dosing, Duration	Endpoints	Status	Results
1	C57Bl/6J 90-92 weeks	Q2D, 12 weeks Vehicle & multiple dose groups	Muscle force, histology, proteomics, PD biomarker	Completed	 Target Dose max force & increased contraction rate Target Dose greatest reduction in PD biomarker
2	C57Bl/6J 90-92 weeks	Q2D, 12 weeks Vehicle & multiple dose groups	Muscle force , PD biomarker	Completed	 All doses stat. sign. Target Dose greatest reduction in PD biomarker

Positive Proteomic Data From Study #1:

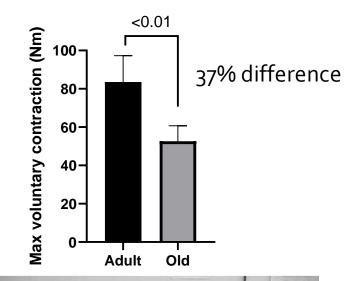
- ✓ Identified effects of MF-300 on the aged muscle proteome in mice
- ✓ Compared with human proteomic and genomic data, elucidated translational potential for MF-300's mechanism

Translational Model: Age Related Decline in Plantar Flexor (Calf Muscle) Force

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Male Old (N=11): 61-74 y.o.



Adult (N=12): 19-24 y.o.

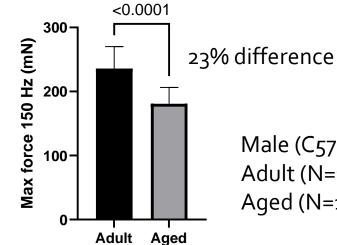
Activities of Daily Living:

- Pressing car pedals
- Extending body to reach
- Walking

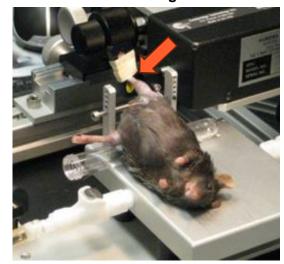
Graph generated from data published in Ochala et al., Exp Ger, 2004



Maximal voluntary contraction

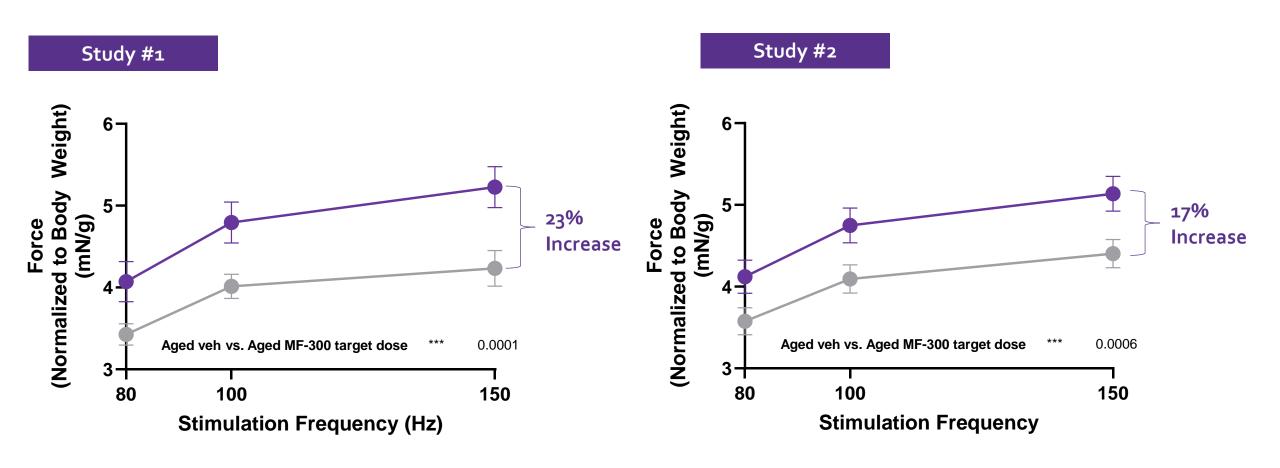


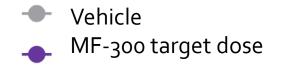
Male (C₅₇Bl/6J) Adult (N=15): 12 m.o. Aged (N=18): 23 m.o.



Electrical nerve-evoked contraction

Mouse is anaesthetized Image from: https://aurorascientific.com/somet imes-two-is-better-than-one/

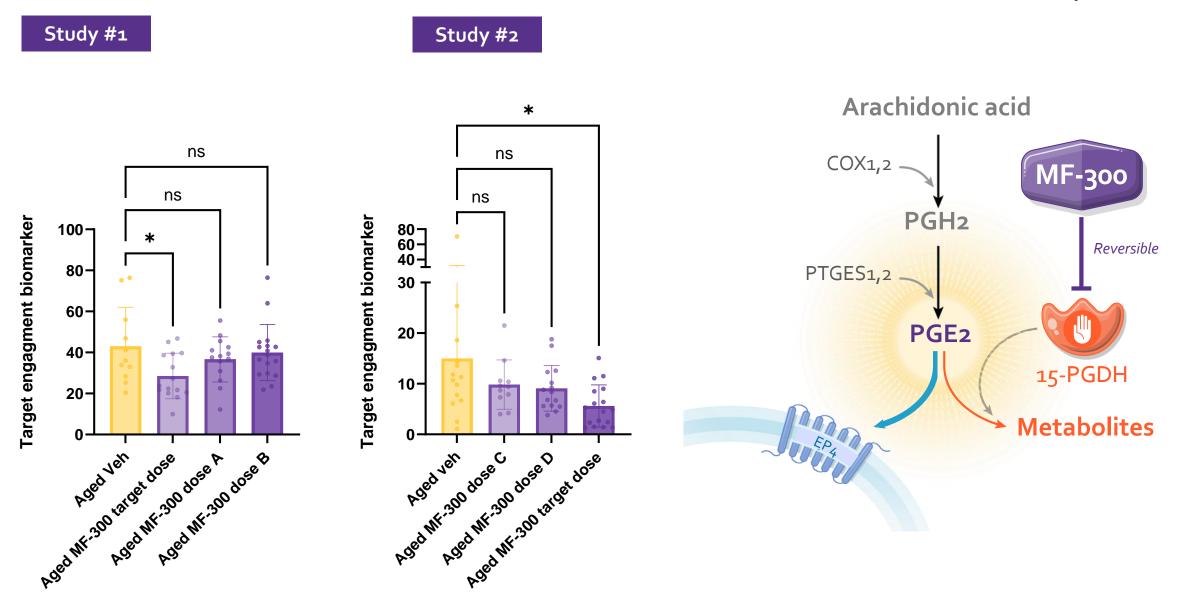




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MF-300 Target Dose Significant Effect on Target Engagement Biomarker

— 🧲 Epirium Bio



MF-300 Potential to Provide Substantial Benefit to Sarcopenia Patients

"Many older people highly value their independence with the desire outweighing other needs. Individuals go to great lengths to achieve independence...."

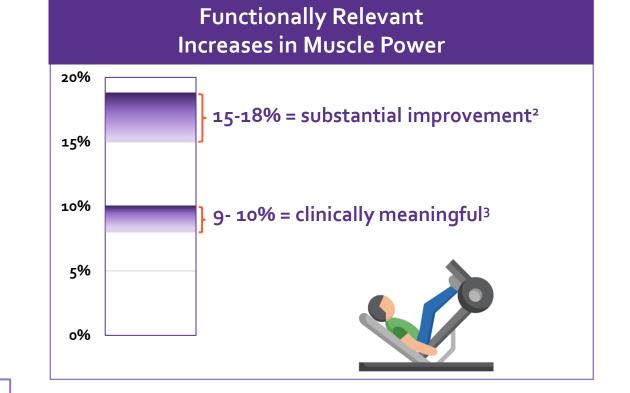
-Older Adults' Perspective of Independence Through Time: Results of a Longitudinal Interview Study¹

"A significant number of sarcopenia patients are on the cusp of losing their independence. If MF-300's preclinical efficacy results are replicated in the clinic, MF-300 should provide a clinically substantial improvement, allowing sarcopenia patients to remain independent."

-Prof. Roger A. Fielding, Ph.D, Senior Scientist & Team Lead, Human Nutrition Research Center on Aging, Tufts University

Leg Power Dependent Key Functional ADLs:

- Climbing stairs, Getting out of a chair, Bathing Reflective Efficacy Endpoints (Leg Power):
- Stair Climb, Double Leg Press, Knee Extension, SPPB*



Muscle Power = Muscle Force × Muscle Velocity

¹Taylor et al, *The Genrontologist* , 2023 ²Kirn et al., 2016; ³Kirn et al., 2016

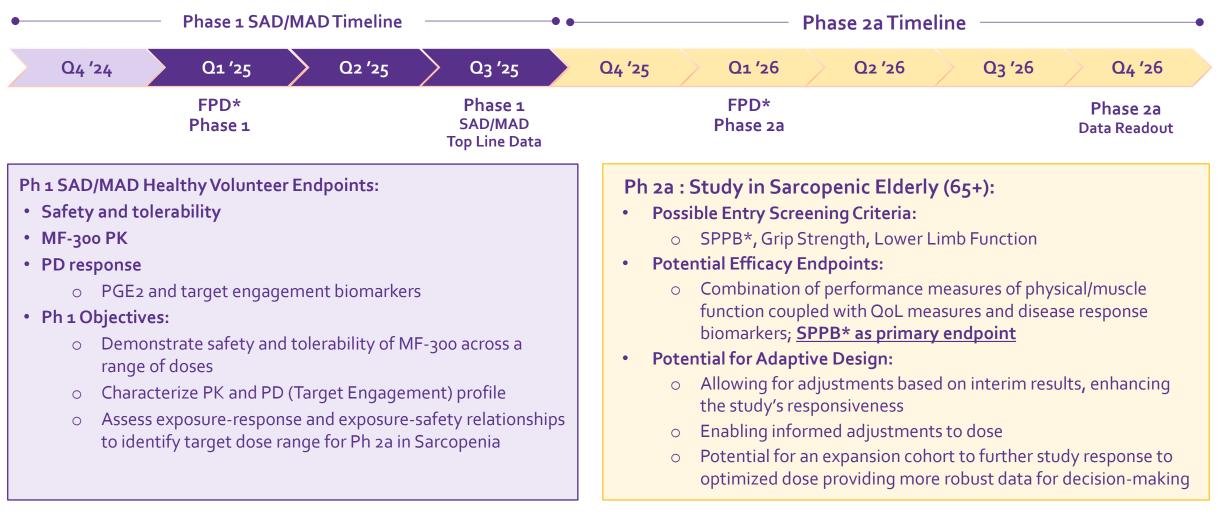
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*Short Physical Performance Battery

MF-300: On-track to Deliver Transformational Clinical Value

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MF-300 "First-in-Class" Oral Sarcopenia Tx: Ph 1 w/ TE* biomarker Q3 '25, Ph 2a Efficacy Q4 '26

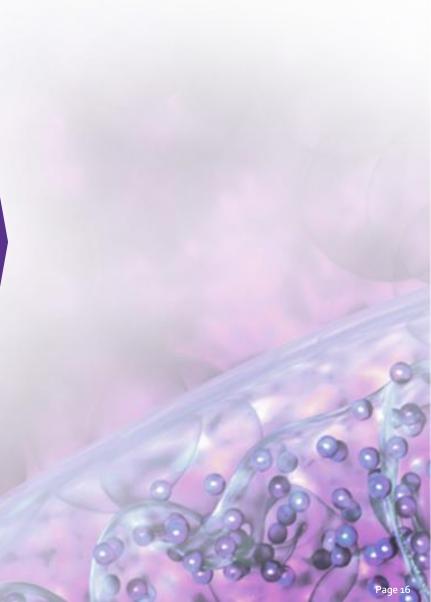


Epirium Platform: Addressing High Value Indications with Unmet Medical Needs

DISEASE	Oral Compound	DISCOVERY PRECLINICAL PHASE 1	PHASE 2
Sarcopenia	MF-300	into a "first stage comp sarcopenia	pirium transforms -in-class" clinical pany targeting a large unmet need A approved therapies
Fibrosis	NCE1		
Neuromuscular	NCE2		

Supportive Material Information:

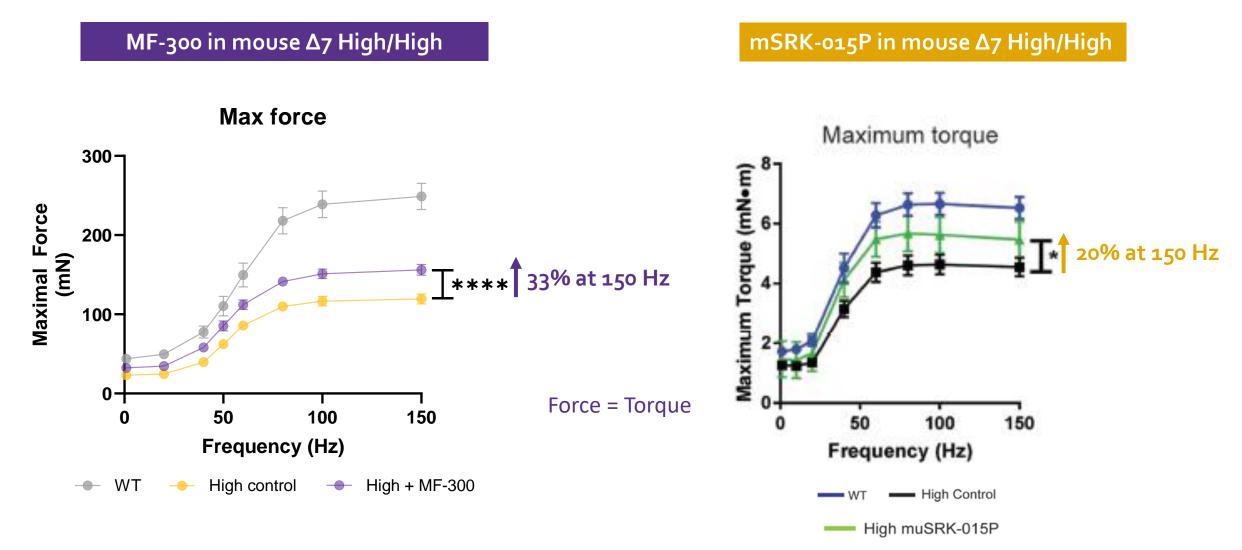
- Current Ownership
- MF-300 Comparison to murine Apitegromab in Delta 7 Mice





MF-300 Attractive Competitive Profile Compared to mSRK-015P in SMNA7 + SMN Upregulator

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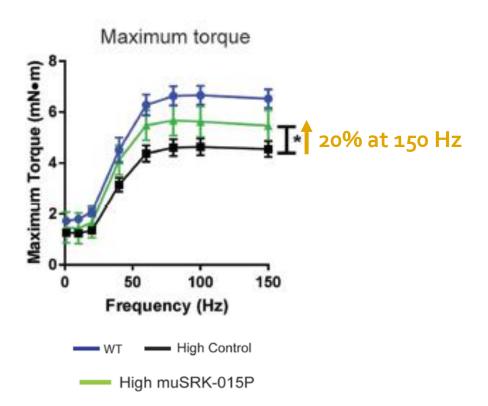
MYOLOGICA

Long et al., Hum Mol Gen, 2019

Scholar Rock's Preclinical and Clinical Data Set Precedent for Translation of Efficacy

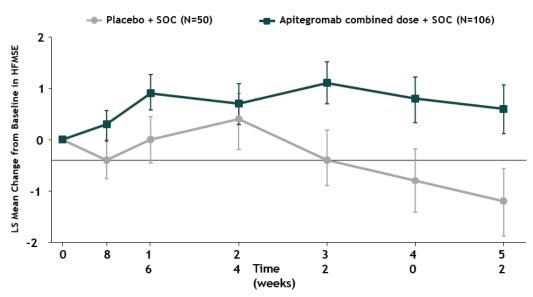
Demonstrates that a 20% increase in isometric plantar flexor force in mice translates to clinical benefit

mSRK-015P in mouse Δ 7 High/High



Apitegromab in SMA + SOC (Ph 3 SAPPHIRE)

Least Squares Mean (+/- SE) Change from Baseline in HFMSE Total Score by Visit (MITT Set)



Change from Baseline in HFMSE Total Score

	Analysis	n	Results (vs Placebo, n=50)	Unadjusted P -value		
Primary Analysis	Apitegromab 10+20 mg/kg combined	106	1.8	0.0192*	Achieved Statistical Significance	
	Apitegromab 20 mg/kg	53	1.4	0.1149*		
	Apitegromab 10 mg/kg	53	2.2	0.0121**	🐝 Scholar Rock	

Long et al., Hum Mol Gen, 2016

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